

=> d his

(FILE 'HOME' ENTERED AT 09:10:35 ON 14 SEP 2000)

FILE 'MEDLINE' ENTERED AT 09:10:45 ON 14 SEP 2000

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L1      2 S QUISCENT STEM CELLS OR QUISCENT CELLS
L2      2972 S RETROVIRAL VECTOR OR RETROVIRAL PARTICLE
L3      0 S L1 AND L2
L4      37497 S STEM CELLS
L5      10 S QUISCENT
L6      0 S L4 AND L5
L7      442 S FLT3
L8      2942 S FLT3 OR STEM CELL FACTOR
L9      1425 S L4 AND L8
L10     36166 S FUSION PROTEIN
L11     86 S L9 AND L10
L12     7 S L2 AND L11

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FILE 'CAPLUS, USPATFULL, BIOSIS, EMBASE' ENTERED AT 09:15:52 ON 14 SEP 2000

FILE 'CAPLUS, USPATFULL, BIOSIS, EMBASE, MEDLINE' ENTERED AT 09:16:04 ON 14 SEP 2000

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L13     56 S L12
L14     55 DUP REM L13 (1 DUPLICATE REMOVED)

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=> logoff

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

| | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 153.02 | 159.87 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -0.56 | -0.56 |

STN INTERNATIONAL LOGOFF AT 09:30:43 ON 14 SEP 2000

LREP Feit, Irving N.; Sheets, Eric J.; Weiss, Laura S.
CLMN Number of Claims: 4
ECL Exemplary Claim:
DRWN 4 Drawing Figure(s) 14 Drawing Page(s)
LN.CNT 1610

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Isolated mammalian nucleic acid molecules encoding receptor protein tyrosine kinases expressed in primitive hematopoietic cells and not expressed in mature hematopoietic cells are provided. Also included are the receptors encoded by such nucleic acid molecules; the nucleic acid molecules encoding receptor protein tyrosine kinases having the sequences shown in FIG. 1 (flk-2) and FIG. 2 (flk-1); the receptor protein tyrosine kinases having the amino acid sequences shown in FIG. 1 (flk-2) and FIG. 2 (flk-1); ligands for the receptors; nucleic acid sequences that encode the ligands; and methods of stimulating the proliferation of primitive mammalian hematopoietic stem cells comprising contacting the stem cells with a ligand that binds to a receptor protein tyrosine kinase expressed in primitive mammalian hematopoietic cells and not expressed in mature hematopoietic cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

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L12 7 S L2 AND L11

FILE 'CAPLUS, USPATFULL, BIOSIS, EMBASE' ENTERED AT 09:15:52 ON 14 SEP 2000

FILE 'CAPLUS, USPATFULL, BIOSIS, EMBASE, MEDLINE' ENTERED AT 09:16:04 ON 14 SEP 2000

L13 56 S L12
L14 55 DUP REM L13 (1 DUPLICATE REMOVED)

LN.CNT 10318

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides compositions and method, for utilizing recombinant alphavirus vectors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 21 OF 55 USPATFULL

AN 1998:150460 USPATFULL

TI Peripheralization of hematopoietic stem cells

IN Papayannopoulou, Thalia, Seattle, WA, United States

PA Board of Regents University of Washington, Seattle, WA, United States (U.S. corporation)

PI US 5843438 19981201

WO 9411027 19950526

AI US 1995-436339 19950713 (8)

WO 1993-US11060 19931115

19950713 PCT 371 date

19950713 PCT 102(e) date

RLI Continuation-in-part of Ser. No. US 1992-977702, filed on 13 Nov 1992, now abandoned

DT Utility

EXNAM Primary Examiner: Scheiner, Toni R.; Assistant Examiner: Johnson, Nancy A.

CLMN Number of Claims: 14

ECL Exemplary Claim: 1

DRWN 18 Drawing Figure(s); 12 Drawing Page(s)

LN.CNT 1221

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to in vivo peripheralization of CD34.sup.+ cells by administering anti-VLA-4 antibodies or anti-VCAM-1 antibodies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 22 OF 55 USPATFULL

AN 1998:150447 USPATFULL

TI Methods of stimulating hematopoietic cells with flt3-ligand

IN Lyman, Stewart D., Seattle, WA, United States

Beckmann, M. Patricia, Poulsbo, WA, United States

PA Immunex Corporation, Seattle, WA, United States (U.S. corporation)

PI US 5843423 19981201

AI US 1997-993962 19971218 (8)

RLI Continuation of Ser. No. US 1995-444625, filed on 19 May 1995, now abandoned which is a division of Ser. No. US 1994-243545, filed on 11 May 1994, now patented, Pat. No. US 5554512, issued on 6 Sep 1996 which is a continuation-in-part of Ser. No. US 1994-209502, filed on 7 Mar 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-162407, filed on 3 Dec 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-111758, filed on 25 Aug 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-106463, filed on 12 Aug 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-68394, filed on 24 May 1993

DT Utility

EXNAM Primary Examiner: Feisee, Lila; Assistant Examiner: Gambel, Phillip

LREP Malaska, Stephen L.

CLMN Number of Claims: 17

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2056

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Ligands for flt3 receptors capable of transducing self-renewal signals to regulate the growth, proliferation or differentiation of progenitor cells and stem cells are disclosed. The invention is directed to flt3-L as an isolated protein, the DNA encoding the flt3-L, host cells transfected with cDNAs encoding flt3-L, compositions comprising flt3-L, methods of improving gene transfer to a mammal using flt3-L, and methods of improving transplantations using flt3-L. Flt3-L finds use in treating patients with anemia, AIDS and various cancers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5723287 19980303
 WO 9406920 19940331
 AI US 1995-381960 199503 (8)
 WO 1993-GB1992 19930922
 19950503 PCT 371 date
 19950503 PCT 102(e) date
 PRAI GB 1992-20010 19920922
 GB 1993-4962 19930311
 DT Utility
 EXNAM Primary Examiner: Elliott, George C.; Assistant Examiner: Schwartzman, Robert
 LREP Williams, Kathleen Madden
 CLMN Number of Claims: 24
 ECL Exemplary Claim: 1
 DRWN 10 Drawing Figure(s); 10 Drawing Page(s)
 LN.CNT 2194

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB We have made retrovirus particles displaying a functional antibody fragment. We fused the gene encoding an antibody fragment directed against a hapten with that encoding the viral envelope protein (Pr80env) of the ecotropic Moloney murine leukemia virus. The fusion gene was co-expressed in ecotropic retroviral packaging cells with a retroviral plasmid carrying the neomycin phosphotransferase gene (neo), and retroviral particles with specific hapten binding activities were recovered. Furthermore the hapten-binding particles were able to transfer the neo gene and the antibody-envelope fusion gene to mouse fibroblasts. In principle, the display of antibody fragments on the surface of recombinant retroviral particles could be used to target virus to cells for gene delivery, or to retain the virus in target tissues, or for the construction of libraries of viral display packages.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 34 OF 55 USPATFULL
 AN 1998:1905 USPATFULL
 TI Nucleic Acid Encoding novel protein tyrosine kinase
 IN Civin, Curt I., Baltimore, MD, United States
 Small, Donald, Baltimore, MD, United States
 Safford, Meredith G., Baltimore, MD, United States
 PA The Johns Hopkins University School of Medicine, Baltimore, MD, United States (U.S. corporation)
 PI US 5705625 19980106
 AI US 1994-357598 19941215 (8)
 DT Utility
 EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Teng, Sally P.
 LREP Fish & Richardson, P.C.
 CLMN Number of Claims: 5
 ECL Exemplary Claim: 1
 DRWN 17 Drawing Figure(s); 13 Drawing Page(s)
 LN.CNT 1976

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel protein tyrosine kinase, JAK3, and a polynucleotide sequence encoding JAK3 polypeptide are disclosed herein. JAK3 is a new member of the JAK family of protein tyrosine kinases which are important in regulation of cellular proliferation and differentiation. Also disclosed are therapeutic methods utilizing JAK3 polypeptide and polynucleotide sequences.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 35 OF 55 MEDLINE
 AN 1998241413 MEDLINE
 DN 98241413
 TI Delayed targeting of cytokine-nonresponsive human bone marrow CD34(+) cells with retrovirus-mediated gene transfer enhances transduction efficiency and long-term expression of transduced genes.
 AU Veena P; Traycoff C M; Williams D A; McMahon J; Rice S; Cornetta K; Srouf E F
 CS Division of Hematology/Oncology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, USA.
 NC R01 HL55716 (NHLBI)

PO1 CA59348 (NCI)
 P50 DK49218 (NIDDK)
 SO BLOOD, (1998 May 15) 91 (10) 3693-701.
 Journal code: A8G. ISSN: 0006-4971.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
 EM 199808
 EW 19980803
 AB Primitive hematopoietic progenitor cells (HPCs) are potential targets for treatment of numerous hematopoietic diseases using retroviral-mediated gene transfer (RMGT). To achieve high efficiency of gene transfer into primitive HPCs, a delicate balance between cellular activation and proliferation and maintenance of hematopoietic potential must be established. We have demonstrated that a subpopulation of human bone marrow (BM) CD34(+) cells, highly enriched for primitive HPCs, persists in culture in a mitotically quiescent state due to their cytokine-nonresponsive (CNR) nature, a characteristic that may prevent efficient RMGT of these cells. To evaluate and possibly circumvent this, we designed a two-step transduction protocol using neoR-containing vectors coupled with flow cytometric cell sorting to isolate and examine transduction efficiency in different fractions of cultured CD34(+) cells. BM CD34(+) cells stained on day 0 (d0) with the membrane dye PKH2 were prestimulated for 24 hours with **stem cell factor** (SCF), interleukin-3 (IL-3), and IL-6, and then transduced on fibronectin with the **retroviral vector LNL6** on d1. On d5, half of the cultured cells were transduced with the **retroviral vector G1Na** and sorted on d6 into cytokine-responsive (d6 CR) cells (detected via their loss of PKH2 fluorescence relative to d0 sample) and d6 CNR cells that had not divided since d0. The other half of the cultured cells were first sorted on d5 into d5 CR and d5 CNR cells and then infected separately with G1Na. Both sets of d5 and d6 CR and CNR cells were cultured in secondary long-term cultures (LTCs) and assayed weekly for transduced progenitor cells. Significantly higher numbers of G418-resistant colonies were produced in cultures initiated with d5 and d6 CNR cells compared with respective CR fractions ($P < .05$). At week 2, transduction efficiency was comparable between d5 and d6 transduced CR and CNR cells ($P > .05$). However, at weeks 3 and 4, d5 and d6 CNR fractions generated significantly higher numbers of neoR progenitor cells relative to the respective CR fractions ($P < .05$), while no difference in transduction efficiency between d5 and d6 CNR cells could be demonstrated. Polymerase chain reaction (PCR) analysis of the origin of transduced neoR gene in clonogenic cells demonstrated that mature progenitors (CR fractions) contained predominantly LNL6 sequences, while more primitive progenitor cells (CNR fractions) were transduced with G1Na. These results demonstrate that prolonged stimulation of primitive HPCs is essential for achieving efficient RMGT into cells capable of sustaining long-term in vitro hematopoiesis. These findings may have significant implications for the development of clinical gene therapy protocols.

L14 ANSWER 36 OF 55 MEDLINE
 AN 1998139478 MEDLINE
 DN 98139478
 TI Inverse targeting of **retroviral vectors**: selective gene transfer in a mixed population of hematopoietic and nonhematopoietic cells.
 AU Fielding A K; Maurice M; Morling F J; Cosset F L; Russell S J
 CS Cambridge Centre for Protein Engineering and Cambridge University Dept Haematology, MRC Centre, Cambridge, UK.
 SO BLOOD, (1998 Mar 1) 91 (5) 1802-9.
 Journal code: A8G. ISSN: 0006-4971.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
 EM 199805
 AB We previously reported that **retroviral vectors** displaying epidermal growth factor (EGF) as part of a chimeric envelope glycoprotein are sequestered upon binding to EGF receptor (EGFR)-positive target cells, leading to loss of infectivity. In the current study, we have displayed **stem cell factor** (SCF) on

beta-galactosidase-transducing ecotropic and amphotropic retroviral vector particles as a factor Xa protease-cleavable N-terminal extension of the envelope glycoprotein. Viral incorporation of the SCF chimeric envelopes was demonstrated by immunoblotting of pelleted virions and their specific attachment to Kit receptors was demonstrated by flow cytometry. Gene transfer studies showed that when SCF was displayed on an amphotropic envelope, the infectivity of the SCF-displaying vectors was selectively inhibited on Kit-expressing cells, but could be restored by adding soluble SCF to block the Kit receptors or by cleaving the displayed SCF domain from the vector particles with factor Xa protease. The host range properties of EGF-displaying and SCF-displaying vectors were then compared in cell mixing experiments. When EGFR-positive cancer cells and Kit-positive hematopoietic cells were mixed and exposed to the different engineered vector particles, the cancer cells were selectively transduced by the SCF-displaying vector and the hematopoietic cells were selectively transduced by the EGF-displaying vector. Retroviral display of polypeptide growth factors can therefore provide the basis for a novel inverse targeting strategy with potential use for selective transduction of hematopoietic or nonhematopoietic cells (eg, cancer cells) in a mixed cell population.

L14 ANSWER 37 OF 55 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1

AN 1998:258434 CAPLUS

DN 129:36923

TI Retroviral vector targeting human cells via c-Kit-stem cell factor interaction

AU Yajima, Toshitaka; Kanda, Tadahito; Yoshiike, Kunito; Kitamura, Yoshihiro

CS The Heart Institute of Japan, Tokyo Women's Medical College, Tokyo, 162, Japan

SO Hum. Gene Ther. (1998), 9(6), 779-787

CODEN: HGTHE3; ISSN: 1043-0342

PB Mary Ann Liebert, Inc.

DT Journal

LA English

AB Targeted gene transfer into hematopoietic stem cells

by retroviral vectors would greatly facilitate the development of in vivo strategies for stem cell gene therapy. We engineered a recombinant retroviral vector that can target human cells expressing a c-Kit receptor via a ligand-receptor interaction. The ecotropic (Moloney murine leukemia virus) envelope protein was modified by insertion of a sequence encoding the N-terminal 161 amino acids of murine stem cell factor (mSCF), the ligand for murine c-Kit. The chimeric envelope protein was correctly processed and incorporated into viral particles as efficiently as the wild-type envelope protein. Virions pseudotyped with the chimeric envelope proteins bound to 293 cells expressing murine c-Kit (293KIT) preferentially; however, they could not transduce any c-Kit-pos. cells under conventional conditions. They could transduce 293KIT cells in the presence of chloroquine, and HEL cells expressing human c-Kit on a fibronectin fragment (CH296)-coated dish. The fact that recombinant mSCF in the medium at the time of transduction greatly reduced the efficiency of both gene deliveries implies that the vector utilized the mSCF-c-Kit interaction for the initial step of transduction in either case. The vector may prove useful for targeting cells expressing c-Kit on their surface.

L14 ANSWER 38 OF 55 USPATFULL

AN 97:114926 USPATFULL

TI Peripheralization of hematopoietic stem cells

IN Papayannopoulou, Thalia, 3336 Cascadia Ave. South, Seattle, WA, United States 98144

PI US 5695755 19971209

AI US 1995-463128 19950605 (8)

RLI Division of Ser. No. US 1993-436339, filed on 15 Nov 1993 which is a continuation-in-part of Ser. No. US 1992-977702, filed on 13 Nov 1992, now abandoned

DT Utility

EXNAM Primary Examiner: Feisee, Lila; Assistant Examiner: Johnson, Nancy A.

LREP Flynn, Kerry A.

CLMN Number of Claims: 10

ECL Exemplary Claim: 1